TYPHOID FEVER
(Enteric Fever, Typhus Abdominalis)

✓DISEASE AND EPIDEMIOLOGY

Clinical Description:

Typhoid fever is a systemic bacterial disease**.** Initial symptoms typically include sustained fever, anorexia, lethargy, malaise, dull continuous headache, and a non-productive cough. Vomiting and diarrhea are typically absent, but constipation is frequently reported. During the second week of illness, there is often a protracted fever and mental dullness. After the first week or so, many cases develop a maculopapular rash on the trunk and upper abdomen ("rose spots"). Other symptoms can include intestinal bleeding, slight deafness, and parotitis. Mild and atypical infections are common, as are relapses.

Causative Agent:

Typhoid fever is caused by a bacterium called *Salmonella typhi*. While many other *Salmonella* species cause disease, typhoid fever has a very different clinical presentation. A new classification for *Salmonella* has been adopted based on DNA relatedness. This new nomenclature recognizes only two species: *Salmonella bongori* and *Salmonella enterica*, with all human pathogens regarded as serovars within the subspecies of *S. enterica*. The proposed nomenclature would change *S. typhi* to *S. enterica* serovar Typhi, abbreviated *S.* Typhi.

Differential Diagnosis:

The differential diagnosis for typhoid fever includes paratyphoid fever, parenteric fever, brucellosis, malaria, subacute bacterial endocarditis, kala azar, liver amebiasis, and typhus.

Laboratory identification:

Isolation of *S.* Typhi from clinical specimens is the preferred method for laboratory diagnosis. Blood cultures in the first week of disease and stool and urine samples thereafter are the appropriate specimens. *S.* Typhi can be also cultured from the bone marrow; in fact, this is the single most sensitive method of isolating of *S.* Typhi. The serologic test (Widal test) is generally of little diagnostic value.

> **UPHL:** The Utah Public Health Laboratory accepts stool specimens for isolation and serotyping. All isolates must be submitted to UPHL.

Treatment:

Typhoid fever is treated with antibiotics. Ampicillin, amoxicillin, cefotaxime, ceftriaxone, chloramphenicol, TMP-SMX, and fluoroquinolines are all appropriate treatments. The drug of choice, route of administration, and duration of therapy are based on the susceptibility of the organism, site of infection, host, and clinical response. A person will usually recover in 2-3 days with prompt antibiotic treatment. Relapse is common after therapy, and retreatment is indicated in these cases.

Case fatality:
As many as 10–20% of untreated infections may be fatal. Less than 1% of infections are fatal with prompt antibiotic treatment.

Reservoir:
Humans are the only reservoir for *S.* Typhi. Chronic carriers are the most important reservoir for *S.* Typhi. About 2–5% of cases become chronic carriers, some after symptomatic infection.

Transmission:
S. Typhi is transmitted via the fecal-oral route, either directly from person-to-person or by ingestion of food or water contaminated with feces or urine. Shellfish harvested from sewage-contaminated water are potential vehicles, as are fruits and vegetables grown in soil fertilized with human waste in developing countries. Transmission can also occur from person to person through certain types of sexual contact (e.g., oral-anal contact).

Susceptibility:
Anyone can get typhoid fever if they drink water or eat food contaminated with the *S.* Typhi bacteria. Travelers visiting developing countries are at greatest risk for getting typhoid fever.

Incubation period:
The incubation period for typhoid fever is usually 8-14 days, with a range of 3 days to 2 months depending on the infecting dose.

Period of communicability:
Typhoid fever is communicable for as long as the infected person excretes *S.* Typhi in the feces or urine. This usually begins about a week after onset of illness, continues through convalescence, and occurs for a variable period thereafter. If a carrier state develops, excretion of *S.* Typhi could be permanent.

Epidemiology:
The annual incidence of typhoid fever worldwide is approximately 17 million cases, with an estimated 600,000 deaths. In the US, less than 500 cases occur each year, and 70% of these are acquired while traveling internationally. Over the past ten years, travelers to Asia, Africa, and Latin America have been especially at risk. Antimicrobial-resistant strains are becoming increasingly prevalent. Outbreaks have occurred in the US from food brought here from other countries. Despite suggestions to the contrary, outbreaks do not occur as a result of floods or other disasters in countries, such as the US, that are not endemic for typhoid. There are an average of one to two cases of typhoid reported in Utah each year.

✓PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

- Investigate all suspect cases of disease and fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention
- Identify clusters or outbreaks of this disease and determine the source.
- Identify cases and sources to prevent further transmission.

Prevention:

Environmental Measures

Implicated food items must be removed from consumption. A decision about testing implicated food items can be made in consultation with the enteric epidemiologist at UDOH and UPHL.

The general policy of UPHL is to test only food samples implicated in suspected outbreaks, not in single cases (except when botulism is suspected). If holders of food implicated in single case incidents would like their food tested, they may be referred to a private laboratory that will test food or store the food in their freezer for a period of time in case additional reports are received. However, in certain circumstances, a single, confirmed case with leftover food that had been consumed within the incubation period may be considered for testing.

Personal Preventive Measures/Education

To avoid exposure to *Salmonella* Typhi, persons should:

- Always wash their hands thoroughly with soap and water before eating or preparing food, after using the toilet, after changing diapers, and after touching pets or other animals (especially reptiles).
- Wash the child's hands as well as their own hands after changing diapers, and dispose of diapers in a closed-lid garbage can.
- Wash hands thoroughly and frequently when ill with diarrhea or when caring for someone with diarrhea. Hands should be scrubbed for at least 15–20 seconds after cleaning the bathroom; after using the toilet or helping someone use the toilet; after changing diapers; before handling food; and before eating.

Discuss transmission risks that may result from oral-anal sexual contact. Latex barrier protection (e.g., dental dam) may prevent the spread of *Salmonella* to a case's sexual partners and may prevent exposure to and transmission of other fecal-oral pathogens.

International Travel

Persons traveling to typhoid endemic areas should consider vaccination against typhoid fever. They should check with their health care provider or a travel clinic for vaccine options. This needs to be done in advance so that the vaccine has time to take effect. Recommend the following to travelers:

- "Boil it, cook it, peel it, or forget it." Avoid foods and beverages from street vendors.

- Drink only bottled or boiled water, keeping in mind that bottled carbonated water is safer than non-carbonated bottled water.
- Ask for drinks without ice, unless the ice is made from bottled or boiled water.
- Avoid popsicles and flavored ices that may have been made with contaminated water.
- Eat foods that have been thoroughly cooked and are still hot and steaming.
- Avoid raw vegetables and fruits that cannot be peeled. Vegetables like lettuce are easily contaminated and are very hard to thoroughly wash.

Chemoprophylaxis:
Vaccination of household contacts of active cases is of limited value. However, vaccination of household contacts of chronic carriers is beneficial.

Vaccine:
Two vaccines for typhoid fever are currently licensed in the US. An oral vaccine consisting of 4 capsules taken every 2 days is available for persons 6 years of age and older. The second vaccine consists of A single intramuscular dose for persons 2 years of age and older. The vaccine efficacies range from 50-80%, and thus travelers must still exercise caution when consuming local foods and beverages. Additionally, typhoid vaccines lose effectiveness after several years, and booster doses are necessary.

Isolation and quarantine requirements:
Isolation: Food handlers with typhoid must be excluded from work. After diarrhea has resolved, food handlers may only return to work after producing 3 consecutive negative stool specimens, each taken no less than 24 hours apart. If the case has been treated with an antimicrobial, the stool specimen should not be collected until at least 48 hours after cessation of therapy.
NOTE: A food handler is any person directly preparing or handling food. This can include a patient care or childcare provider.
Hospital: Enteric precautions.
Quarantine: All food handling facility employees, symptomatic or asymptomatic, who are contacts of a typhoid case should be considered the same as a case and should be handled in the same fashion.

✓CASE INVESTIGATION
Reporting:
All cases of typhoid should be reported immediately to public health.

Case definition:
Typhoid Fever *(Salmonella* Typhi*)* (1997):
Clinical description
An illness caused by *Salmonella* Typhi that is often characterized by insidious onset of sustained fever, headache, malaise, anorexia, relative bradycardia, constipation or diarrhea, and nonproductive cough. However, many mild and atypical infections occur. Carriage of *S.* Typhi may be prolonged.

Laboratory criteria for diagnosis

Isolation of *S.* Typhi from blood, stool, or other clinical specimen

Case classification

Probable: A clinically compatible case that is epidemiologically linked to a confirmed case in an outbreak.

Confirmed: A clinically compatible case that is laboratory confirmed.

Comment

Isolation of the organism is required for confirmation. Serologic evidence alone is not sufficient for diagnosis. Asymptomatic carriage should not be reported as typhoid fever. Isolates of *S.* Typhi are reported to the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC, through the Public Health Laboratory Information System.

Case Investigation Process:

- Food handlers should be excluded from work until their symptoms are resolved and they can produce 3 consecutive negative stool specimens.
- Investigate cases and contacts for carriage.
- Assure isolate submission to UPHL.

Outbreaks:

CDC defines a food-borne outbreak as, “an incident in which two or more persons experience a similar illness resulting from the ingestion of a common food”. In order to confirm an outbreak of typhoid, the organism must be isolated from clinical specimens from at least 2 ill persons or from an epidemiologically implicated food. The source of the infection should be identified and measures to identify additional ill persons and/or to remove the source from consumers should be taken. Control of person-to-person transmission requires special emphasis on personal cleanliness and sanitary disposal of feces.

Identification of case contacts and management:

Daycare

Since typhoid fever may be transmitted from person to person through fecal-oral transmission, it is important to follow up on cases of typhoid fever in a daycare setting. General recommendations include:

- Children or staff members in a daycare center who test positive for *S.* Typhi should be excluded until 3 consecutive stool cultures taken 48 hours apart (and no sooner than 48 hours after the cessation of antibiotic therapy) are negative.
- Staff and attendees may be required to submit stool specimens for testing and may be subject to exclusion.

School

Since typhoid fever may be transmitted from person to person through fecal-oral transmission, it is important to follow up on cases of typhoid fever in a school setting.

- Students or staff with *S.* Typhi who are experiencing symptoms, such as diarrhea, fever, and abdominal pain, should be excluded until symptoms have resolved.

- Students or staff with *S.* Typhi who do not handle food, have no symptoms, and are not otherwise ill may remain in school if special precautions are taken.
- If a case of *S.* Typhi occurs in a kindergarten, 1st grade, or a preschool class (where hygiene may not be optimal), more stringent control measures may be indicated.
- Students or staff who handle food and have a *S.* Typhi infection (symptomatic or not) must not prepare or handle food for others until they have 3 negative stool specimens taken 24 hours apart (and no sooner than 48 hours after the cessation of antibiotic therapy).

Community Residential Programs

Actions taken in response to a case of *S.* Typhi in community residential programs will depend on the type of program and the level of functioning of the residents.

In long-term care facilities, residents with *S.* Typhi should be placed on standard (including enteric) precautions until symptoms subside and they test negative with three consecutive stool specimens. Close contacts in the long-term care facility, including staff and roommates, should also be tested. If positive, they should be placed on enteric precautions until they test negative with three stool cultures. Staff members with cultures positive for *S.* Typhi and who give direct patient care (e.g., feed patients, provide mouth or denture care, administer medications), are considered food handlers and must be excluded until they produce three negative stool specimens.

In residential facilities for the developmentally disabled, staff and clients with *S.* Typhi must refrain from handling or preparing food for other residents until their symptoms have subsided and until they produce 3 negative stool specimens, taken 24 hours apart and no sooner than 48 hours after the cessation of antibiotic therapy. Other close contacts in the facility should be tested as well, and if positive, should be subject to the same restrictions stated above.

✓REFERENCES

Centers for Disease Control, Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR 46 (RR-10), 1997.l

Control of Communicable Diseases Manual (18th Edition), Heymann, D.L., Ed; 2004.

Red Book: 2003 Report of the Committee on Infectious Diseases (26th Edition), Larry K. Pickering MD, Ed; 2003.

Principles and Practice of Infectious Disease (6th Edition), Gerald L. Mandell, John E. Bennett, and Raphael Dolin Eds; 2005.

Massachusetts Department of Public Health, Guide to Surveillance, Reporting and Control, 2006.